AMENDMENTS

In the specification:

Please add the following paragraph at page 1, between lines 2 and 3, before "FIELD OF THE INVENTION":

RELATED APPLICATIONS

This application is a continuation-in-part of International Application No. PCT/GB00/03056, which designated the United States and was filed on August 9, 2000, and was published in English, which in turn claims the benefit of U.S. Provisional Application No. 60/181,796, filed on February 11, 2000, and also United Kingdom Application No. 0002856.3, filed February 8, 2000.

B1

Please replace the paragraph at page 9, lines 5-12, with the following paragraph:

Figure 6 shows the stability of cellular integrity (cell numbers) and ultrasound sensitivity during storage at 4°C. Cells were loaded with FITC labelled antibody using a process comprising pre-sensitisation/hypotonic dialysis/electrosensitisation (ES-HD-ES) and at the indicated times cell numbers (▲) were determined by direct counting. The percentage of cells that lysed following exposure to ultrasound was also determined (♦) for each sample. The X-axis represents the time in days, the left Y-axis represents the percentage of cells remaining intact and the right Y-axis represents the percentage lysis observed following exposure to ultrasound.

B2

Please replace the paragraph running from page 42, line 20 to page 43, line 3, with the following paragraph:

B3

In the loading and sensitisation protocol, cells were loaded at a concentration of 1.1mg of antibody per ml of packed cell volume (PCV). 0.1ml aliquots of cells at $7x10^8$ cells/ml were exposed to ultrasound at intensities shown in Figure 8 and samples were analysed for cell lysis by direct counting. In addition, the amount of antibody released following treatment with ultrasound was determined by ELISA analysis of cell supernatants harvested following centrifugation. The results obtained are shown in Figure 8 and they demonstrate that cells were preferentially lysed at ultrasound power densities greater than $2W/cm^2$. Control cells exhibited little or no effect when treated with ultrasound at these power densities. In addition, at and above $2W/cm^2$ antibody payload was detected in supernatants harvested following ultrasound treatment. In addition, when the total amount of antibody released from the cells using ultrasound was compared with that released following hypotonic lysis in 0.01% (v/v) Triton X100 it was found that 77% of the total antibody was released in the former. The remainder could be found in debris that was recovered by centrifugation following ultrasound treatment.

Please replace the paragraph running from page 43, line 28 to page 44, line 8, with the following paragraph:

B4

In these experiments loaded cells contained approximately 1mg of enzyme per ml of packed cell volume. The results obtained following treatment of these preparations with ultrasound are shown in Figure 9. Samples were treated at the indicated power densities as shown and samples were analysed for cell lysis by cell counting. Lysis increased with increasing power density up to a maximum at about $3W/cm^2$. Exposure of control normal cells to similar ultrasound conditions had little or no effect on cell lysis

and this was confirmed by the absence of haemoglobin in supernatants following removal of cells by centrifugation. When supernatants were harvested by centrifugation, following exposure of the sensitised and loaded cells to ultrasound and analysed for enzyme content, it was found that increasing amounts of enzyme were released with increasing power density up to a maximum at $3W/cm^2$.

Please replace the paragraph on page 45, lines 1-6, with the following paragraph:

The results obtained following treatment of these loaded preparations with ultrasound are shown in Figure 10. As with the above two examples, cell lysis of the sensitised and loaded preparation occurs between 2 and 3 W/cm^2. Under these ultrasound conditions there is little or no effect on control erythroyctes. In addition oligonucleotide begins to appear in harvested supernatants between 2 and 3 W/cm^2 demonstrating ultrasound-mediated release of oligonucleotide payload from the vehicle.

Amendments to the specification are indicated in the attached "Marked Up Version of Amendments" (pages i-iii).

In the Claims

Please cancel claims 5-8, 20-25, 27-29 and 33-35 without prejudice, these claims being directed to a non-elected invention. Please also cancel claim 9.

Please amend claims 1-2, 4, 10-12, and 30-32 as follows. Amendments to the claims are indicated in the attached "Marked Up Version of Amendments" (pages iv - v).

1. (Amended) A method of producing a red blood cell comprising an agent the method comprising: a first step of pre-sensitizing a red blood cell *in vitro* or *ex*